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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/898,513	07/03/2001	Gregory J. LaRosa	1855.1052-020	5309

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EXAMINER
SALIMI, ALI REZA

ART UNIT	PAPER NUMBER
1648	15

DATE MAILED: 05/21/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 09/898,513	Applicant(s) LaRosa et al
	Examiner A. R. SALMI	Art Unit 1648

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *Three* MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1) ☒ Responsive to communication(s) filed on *May 12, 2003* .

2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.

3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

Disposition of Claims

4) ☒ Claim(s) *1-7, 9, 10, and 37-57* is/are pending in the application.

4a) Of the above, claim(s) _____ is/are withdrawn from consideration.

5) ☐ Claim(s) _____ is/are allowed.

6) ☒ Claim(s) *1-7, 9, 10, and 37-57* is/are rejected.

7) ☐ Claim(s) _____ is/are objected to.

8) ☐ Claims _____ are subject to restriction and/or election requirement.

Application Papers

9) ☐ The specification is objected to by the Examiner.

10) ☒ The drawing(s) filed on *May 12, 2003* is/are a) ☒ accepted or b) ☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13) ☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a) ☐ All b) ☐ Some* c) ☐ None of:

1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____ .
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

*See the attached detailed Office action for a list of the certified copies not received.

14) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

a) ☐ The translation of the foreign language provisional application has been received.

15) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s). _____
4) ☐ Interview Summary (PTO-413) Paper No(s). _____
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

DETAILED ACTION

Response to Amendment

This is a response to the amendment A, paper No.14, filed 5/12/2003. The filing of Declaration under 37 CFR 1.131 and signed by the inventors is acknowledged. Claims 8, 11-36 have been canceled. Claims 47-57 have been added. Claims 1-7, 9, 10, 37-57 are pending before the examiner.

Please note any grounds of rejection that has not been repeated is removed.

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Claim Rejections - 35 USC § 112

Claims 1-7, 9, 10, 37-57 are rejected under 35 U.S.C. 112, first paragraph, for reasons of record advanced in the previous Office Action mailed 11/8/2002. Applicants argue that in the instant application Applicants have provided a substantial amount of guidance regarding how to make antibodies commensurate in scope with claimed invention. Applicants assert that the antibody production is well known and directs the Office to page 13 and page 44. Applicants assert they have identified antibody to CCR2. Applicants add that screening large number of antibodies is not undue experimentation. Applicant's argument as part of amendment A, Paper

NO. 14, filed 5/12/2003 has been considered fully, but they are not persuasive. At the onset applicants are reminded that the CCR2 is a G-protein linked seven transmembrane domain. Making antibodies against 7 spanner domain proteins are not routine since the various domains are internal and are not available by routine experimentation. They are simply imbedded in lipid membrane or internally within the cell. Applicants assertion to pages of specification is noted, however, the said pages incorporate by reference entire articles with no specific blaze-mark provided, which are directed to making simple antibodies against known proteins, and are not directed against raising antibodies against 7 spanner proteins. Interestingly, it is noted that in the declaration filed by the applicants under 1.131 as part of Paper No. 12, the said declaration clearly indicates that applicants only raised antibodies against the N-terminal regions and they primarily targeted their efforts toward the N-terminal region. This is not mere coincidence, Applicants directed their effort and energy to the areas where they could easily obtain antibodies which would simply work, and did not target all other regions. Applicants did this not because raising antibodies against all other regions were routine, but because targeting other regions other than N-terminal required undue experimentation. Applicants targeted their efforts to a region that was easily available to make antibodies against. If making antibodies against all regions were as easily achievable as applicants now have the Office believe, then they would have directed their efforts to all regions (emphasis added). Applicants did not address concern raised by the Office in previous action. The question still remains, the specification provides no teaching that other antibodies raised against any other regions except the amino-terminal region would provide the

inhibition of ligand to the receptor. The antibodies might not be capable of inhibiting and would actually induce signaling activity which would induce not only CCR2 activity but also other chemokines. In addition, the antibodies might simply induce cytosolic calcium which would trigger other related cytokine signaling. To answer the concern raised one of ordinary skill in the art would be forced into undue experimentation to enable the full scope of the claimed invention. Applicants are the ones requesting patent protection and for that exclusive protection they should provide adequate teaching so one of ordinary skill in the art can practice the invention absent undue experimentation. Applicants have taught raising antibodies against the N-terminal region and no other regions. Applicants cannot rely on the knowledge of those skilled in the art to enable the claims without providing adequate teaching. Therefore, considering large quantity of experimentation needed, the unpredictability of the field, the state of the art, and breadth of the claims, it is concluded that undue experimentation would be required to enable the intended claim. Many of these factors have been summarized *In re Wands, 858 F.2d 731, USPQ2d 1400 (Fed. Cir. 1988)*. The rejection is maintained.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a **written description** of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-7, 9, 10, 37-57 are rejected under 35 U.S.C. 112, first paragraph, for reasons of record advanced in the previous Office Action mailed 11/8/2002. Applicants argue that it appears the examiner has improperly limited the alleged disclosure of the application to the working examples which were antibodies (1D9 and 8G2) which bind the amino-terminal domain of CCR2. Applicants further assert that there is a strong presumption that an adequate written description of the claimed invention is present when the application is filed. Applicants further assert that original claims were presented upon filing of the parent application. Applicants add, application provided a clear description of antibodies that bind CCR2 and have reduce to practice two embodiments which meet all of the limitations. Applicants conclude that they were in possession of the claimed invention at the time the invention was filed. Applicant's argument as part of amendment A, Paper NO. 14, filed 5/12/2003 has been considered fully, but they are not persuasive. At the onset applicants are reminded that the only reason Applicant(s) were given patent protection in the parent application was because first and foremost they amended their claims and reduced the scope to the antibodies directed against N-terminal regions of CCR2. In addition, the parent application was distinguished because applicants argued convincingly to the Office that their product is distinguishable over the teaching of prior art i.e Lind patent, since the prior art that was cited by the Office taught antibodies to the N-terminal region which did not have antagonistic ability rather the antibody of the prior art induced Ca+ flux and did not show inhibitory effect. Therefore, it is not so much what Applicants thought they were in possession of at the time of filing that had satisfied written description. Rather it was determined ultimately by

the Office, and applicants' own amendment. See the allowed parent claims, as the allowed parent claims are reflective of what applicants were enabled and what they actually possessed. Applicants are also reminded that the Office did not limit the claims to 1D9 and 8G2, rather indicated that the applicants were in possession of antibodies against N-terminal region of CCR2. The question still remains whether or not applicants were in possession of antibodies against all other regions within the seven transmembrane protein of CCR2. The answer is clearly, NO, since the specification does not set forth the structure of any and all antibodies directed to all other regions of CCR2. Since applicants did not raise any antibody against any other regions of CCR2 but the N-terminal region, they could not have been in possession of all types of antibodies, and/or their fragments. The specification does not set forth the metes and bounds of all other antibodies and or their fragments directed to all regions of CCR2, and there is not enough information about it in literature to guide the one of ordinary skill in the art to predict the structure of antibodies to all the other undisclosed regions. Therefore, a written description of the other claimed antibodies should be disclosed to overcome this rejection. Applicants 1.131 declaration is also noted and can be used as evidence that applicants were not in possession of antibodies against any and all region, because applicants only targeted their efforts to raising antibodies against the N-terminal regions. The rejection is maintained.

Double Patenting

Claims 1, 9, 44, 52 are provisionally rejected as claiming the same invention as that of claims 1, 6 of copending Application No. 09/840,459, for reasons of record advanced in the previous Office Action mailed 11/8/2002. Since, the claims are not allowable, the rejection is maintained until such time where no claims are conflicting or a terminal disclaimer is submitted and accepted.

Claim Rejections - 35 USC § 102

Claims 1-7, 9, 10, 37-57 are rejected under 35 U.S.C. 102(e) as being clearly anticipated by Lind et al (US Patent No. 6,084,075), for reasons of record advanced in the previous Office Action mailed 11/8/2002. Applicants argue via a declaration under 1.131 singed by the inventors that demonstrates the conception and subsequent reduction to practice of the claimed invention prior to the effective U.S. filing date of U.S. Patent No. 6,084,075. Applicants conclude that the ,075 patent cannot be considered prior art because the declaration antedate the cited reference. Applicants' argument as part of declaration filed under 1.131 as part of paper No. 12, and amendment A, Paper NO. 14, filed 5/12/2003 have been considered fully, but they are not persuasive. The submission of declaration is not sufficient to antedate the U.S. patent No. 6,084,075, because the previous rejection was made over the claims and teaching and not the disclosure only. It is very clear that the claims of ,075 patent anticipate the broad limitations of the claimed invention. Applicants are once again requested to pay attention to the claims of the

above cited patent. Still further, the declaration does not show the Applicants either conceived and/or reduced to practice the broad invention that is presently before the Office. The entire declaration and submitted Lab Notes spell out experiments and efforts directed against raising antibodies against the N-terminal region (see for example page A-8 of the declaration), incidentally for which applicants have already received patent protection. However, the claims are much broader in scope and are directed to antibodies and binding fragments which were never conceived nor reduced to practice. Hence, it is concluded that first and for most the claims of Lind's et al patent do indeed anticipate the broad limitations of the claimed invention. Second, the declaration does not show either conception nor reduction to practice the antibodies or fragments directed against all regions of CCR2 as now present before the Office. The rejection is respectfully maintained.

Claim Rejections - 35 USC § 102

Claims 1-7, 9, 10, 37-57 are rejected under 35 U.S.C. 102(a) as being clearly anticipated by Frade et al (J. Clin. Invest. 1997) for reasons of record advanced in the previous Office Action mailed 11/8/2002. Applicants argue via a declaration under 1.131 to demonstrate conception of the claimed invention prior to the effective date of Frade et al, coupled with due diligence from the effective date of the above cited article and reduction to practice. Applicants argue in accordance with accepted practice, the dates of the notebook establish conception of the invention. Applicants assert that Farde et al is not available as a reference against the subject

invention under 35 USC § 102 (a). Applicant's argument as part of declaration filed under 1.131 as part of paper No. 12, and amendment A, Paper NO. 14, filed 5/12/2003 have been considered fully, but they are not persuasive. The declaration does not show the Applicants either conceived and/or reduced to practice the broad invention that is presently before the Office. The entire declaration and submitted Lab Notes spell out experiments and efforts directed against raising antibodies against the N-terminal region only. However, the claims are much broader in scope and are directed to antibodies and binding fragments which were never conceived nor reduced to practice. Hence, it is concluded that first and for most Frade et al article do indeed anticipate the broad limitations of the claimed invention. Second, the declaration does not show either conception nor reduction to practice the antibodies or fragments directed against all regions of CCR2. Therefore, the declaration is not deemed sufficient to overcome the rejection. The rejection is respectfully maintained.

Claims 1-7, 9, 10, 37-57 are rejected under 35 U.S.C. 102(a) as being clearly anticipated by Frade et al (J. Immunology, 1997) for reasons of record advanced in the previous Office Action mailed 11/8/2002. Applicants argue via a declaration under 1.131 to demonstrate conception of the claimed invention prior to the effective date of Frade et al, coupled with due diligence from the effective date of the above cited article and reduction to practice. Applicants argue in accordance with accepted practice, the dates of the notebook establish conception of the invention. Applicants assert that Farde et al is not available as a reference against the subject

invention under 35 USC § 102 (a). Applicant's argument as part of declaration filed under 1.131 as part of paper No. 12, and amendment A, Paper NO. 14, filed 5/12/2003 have been considered fully, but they are not persuasive. The declaration does not show the Applicants either conceived and/or reduced to practice the broad invention that is presently before the Office. The entire declaration and submitted Lab Notes spell out experiments and efforts directed against raising antibodies against the N-terminal region only. However, the claims are much broader in scope and are directed to antibodies and binding fragments which were never conceived nor reduced to practice. Hence, it is concluded that first and for most Frade et al article do indeed anticipate the broad limitations of the claimed invention. Second, the declaration does not show either conception nor reduction to practice the antibodies or fragments directed against all regions of CCR2. Therefore, the declaration is not deemed sufficient to overcome the rejection. The rejection is respectfully maintained.

Claims 1-7, 9, 10, 37-57 are rejected under 35 U.S.C. 102(a) as being clearly anticipated by Lind et al (WO 97/31949, 9/4/1997) for reasons of record advanced in the previous Office Action mailed 11/8/2002. Applicants argue via a declaration under 1.131 to demonstrate conception of the claimed invention prior to the effective date of Lind et al, coupled with due diligence from the effective date of the above cited reference and reduction to practice. Applicants argue in accordance with accepted practice, the dates of the notebook establish conception of the invention. Applicants assert that Lind et al is not available as a reference against the subject

invention under 35 USC § 102 (a). Applicant's argument as part of declaration filed under 1.131 as part of paper No. 12, and amendment A, Paper NO. 14, filed 5/12/2003 have been considered fully, but they are not persuasive. The declaration does not show the Applicants either conceived and/or reduced to practice the broad invention that is presently before the Office. The entire declaration and submitted Lab Notes spell out experiments and efforts directed against raising antibodies against the N-terminal region only. However, the claims are much broader in scope and are directed to antibodies and binding fragments which were never conceived nor reduced to practice. Hence, it is concluded that first and for most Lind et al reference do indeed anticipate the broad limitations of the claimed invention. Second, the declaration does not show either conception nor reduction to practice the antibodies or fragments directed against all regions of CCR2. Therefore, the declaration is not deemed sufficient to overcome the rejection. The rejection is respectfully maintained.

NEW GROUNDS OF REJECTION:

Claim Rejections - 35 USC § 112

Claims 44-57 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Claims are vague and indefinite for recitation of "antigen-binding fragment thereof", the intended "binding fragment(s)" is/are not defined. The metes and bounds of the intended

regions are not defined. Applicants argument in support of the claims 44-57 is noted. Applicants assert the analysis of the claims should be performed in light of the specification. Applicants are reminded that the claims have been indeed interpreted in light of the specification and since the specification does not set forth clear definition of the regions wherein an antibody or antibodies can recognize CCR2, the claims are considered to be vague and indefinite. If the various regions are not taught and it is not clearly or easily recognized then the intended "fragments" are indefinite. Applicants have not taught antibodies against all regions and the antigen binding fragments cannot be deciphered from the specification. Still further, although the claims are interpreted in light of the specification, limitations from the specification are not read into the claims. See *In re Van Geuns*, 988 F.2d 1181, 26 USPQ2d 1057 (Fed. Cir. 1993).

No Claims are allowed.

Conclusion

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL.** See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period

will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to A. R. Salimi whose telephone number is (703) 305-7136. The examiner can normally be reached on Monday-Friday from 9:00 Am to 6:00 Pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, James Housel, can be reached on (703) 308-4027. The fax phone number for this Group is (703) 305-3014, or (703) 308-4242.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (703) 308-0196.

A. R. Salimi

5/19/2003

ALI R. SALIMI
PRIMARY EXAMINER